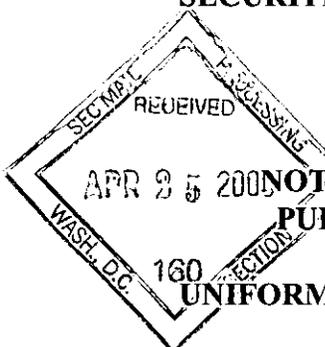


**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549**

**OMB APPROVAL**

OMB Number: 3235-0076  
Expires: March 30, 2008  
Estimated average burden  
hours per form.....1



**FORM D**

**NOTICE OF SALE OF SECURITIES  
PURSUANT TO REGULATION D,  
SECTION 4(6), AND/OR  
UNIFORM LIMITED OFFERING EXEMPTION**

MAY 08 2008  
THOMSON  
FINANCIAL



Name of Offering (  check if this is an amendment and name has changed, and indicate change.)  
Symphony Genesis Holdings, LLC

Filing Under (Check box(es) that apply):       Rule 504       Rule 505       Rule 506       Section 4(6)       ULOE

Type of Filing:       New Filing       Amendment

**A. BASIC IDENTIFICATION DATA**

1. Enter the information requested about the issuer

Name of Issuer (  check if this is an amendment and name has changed, and indicate change.)  
Isis Pharmaceuticals, Inc. BEST AVAILABLE COPY

Address of Executive Offices 1896 Rutherford Road, Carlsbad, CA 92008	(Number and Street, City, State, Zip Code)	Telephone Number (Including Area Code) 760-931-9200
Address of Principal Business Operations (Number and Street, City, State, Zip Code) (if different from Executive Offices) Same		Telephone Number (Including Area Code) Same

Brief Description of Business  
BioPharmaceuticals R&D

Type of Business Organization

corporation       limited partnership, already formed       other (please specify):  
 business trust       limited partnership, to be formed

Actual or Estimated Date of Incorporation or Organization:      Month      Year  
March      1991

Jurisdiction of Incorporation or Organization: (Enter two-letter U.S. Postal Service abbreviation for State:  
CN for Canada; FN for other foreign jurisdiction)       Actual       Estimated  
DE

**GENERAL INSTRUCTIONS**

**Federal:**  
*Who Must File:* All issuers making an offering of securities in reliance on an exemption under Regulation D or Section 4(6), 17 CFR 230.501 et seq. or 15 U.S.C. 77d(6).  
*When to File:* A notice must be filed no later than 15 days after the first sale of securities in the offering. A notice is deemed filed with the U.S. Securities and Exchange Commission (SEC) on the earlier of the date it is received by the SEC at the address given below or, if received at that address after the date on which it is due, on the date it was mailed by United States registered or certified mail to that address.  
*Where to File:* U.S. Securities and Exchange Commission, 450 Fifth Street, N.W., Washington, D.C. 20549.  
*Copies Required:* Five (5) copies of this notice must be filed with the SEC, one of which must be manually signed. Any copies not manually signed must be photocopies of the manually signed copy or bear typed or printed signatures.  
*Information Required:* A new filing must contain all information requested. Amendments need only report the name of the issuer and offering, any changes thereto, the information requested in Part C, and any material changes from the information previously supplied in Parts A and B. Part E and the Appendix need not be filed with the SEC.  
*Filing Fee:* There is no federal filing fee.

**State:**  
This notice shall be used to indicate reliance on the Uniform Limited Offering Exemption (ULOE) for sales of securities in those states that have adopted ULOE and that have adopted this form. Issuers relying on ULOE must file a separate notice with the Securities Administrator in each state where sales are to be, or have been made. If a state requires the payment of a fee as a precondition to the claim for the exemption, a fee in the proper amount shall accompany this form. This notice shall be filed in the appropriate states in accordance with state law. The Appendix to the notice constitutes a part of this notice and must be completed.

**ATTENTION**

**Failure to file notice in the appropriate states will not result in a loss of the federal exemption. Conversely, failure to file the appropriate federal notice will not result in a loss of an available state exemption unless such exemption is predicated on the filing of a federal notice.**

**Potential persons who are to respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB control number.**

**A. BASIC IDENTIFICATION DATA**

2. Enter the information requested for the following:

- Each promoter of the issuer, if the issuer has been organized within the past five years;
- Each beneficial owner having the power to vote or dispose, or direct the vote or disposition of, 10% or more of a class of equity securities of the issuer;
- Each executive officer and director of corporate issuers and of corporate general and managing partners of partnership issuers; and
- Each general and managing partner of partnership issuers.

Check  Promoter  Beneficial Owner  Executive Officer  Director  General and/or Managing Partner  
 Box(es) that Apply:

Full Name (Last name first, if individual)

Federated Investors, Inc.

Business or Residence Address (Number and Street, City, State, Zip Code)

Federated Investors Tower, Pittsburgh, PA 15222-3779

Check  Promoter  Beneficial Owner  Executive Officer  Director  General and/or Managing Partner  
 Box(es) that Apply:

Full Name (Last name first, if individual)

SPENCER R. BERTHELSEN, M.D., F.A.C.P.

Business or Residence Address (Number and Street, City, State, Zip Code)

KELSEY-SEYBOLD CLINIC, 2727 W Holcombe Blvd, 4th Flr, Houston, TX 77025

Check Boxes  Promoter  Beneficial Owner  Executive Officer  Director  General and/or Managing Partner  
 that Apply:

Full Name (Last name first, if individual)

STANLEY T. CROOKE, M.D., PHD

Business or Residence Address (Number and Street, City, State, Zip Code)

ISIS PHARMACEUTICALS, INC., 1896 Rutherford Road, Carlsbad, CA 92008

Check Boxes  Promoter  Beneficial Owner  Executive Officer  Director  General and/or Managing Partner  
 that Apply:

Full Name (Last name first, if individual)

RICHARD D. DIMARCHI, PHD

Business or Residence Address (Number and Street, City, State, Zip Code)

INDIANA UNIVERSITY, Dept of Chemistry, A508, 800 East Kirkwood, Bloomington, IN 47405

Check Boxes  Promoter  Beneficial Owner  Executive Officer  Director  General and/or Managing Partner  
 that Apply:

Full Name (Last name first, if individual)

JOSEPH "SKIP" KLEIN, III

Business or Residence Address (Number and Street, City, State, Zip Code)

GAUSS CAPITAL ADVISORS, LLC, 1724 Hillside Rd, Ste 399, Stevenson, MD 21153

Check Boxes  Promoter  Beneficial Owner  Executive Officer  Director  General and/or Managing Partner  
 that Apply:

Full Name (Last name first, if individual)

FREDERICK T. MUTO, JD

Business or Residence Address (Number and Street, City, State, Zip Code)

COOLEY GODWARD LLP, 4401 Eastgate Mall, San Diego, CA 92121-1909

Check Boxes  Promoter  Beneficial Owner  Executive Officer  Director  General and/or Managing Partner  
 that Apply:

Full Name (Last name first, if individual)

B. LYNNE PARSHALL, JD

Business or Residence Address (Number and Street, City, State, Zip Code)

ISIS PHARMACEUTICALS, INC., 1896 Rutherford Road, Carlsbad, CA 92008

Check  Promoter  Beneficial Owner  Executive Officer  Director  General and/or Managing Partner  
 Box(es) that Apply:

Full Name (Last name first, if individual)

JOHN C. REED, M.D., PHD

Business or Residence Address (Number and Street, City, State, Zip Code)

THE BURNHAM INSTITUTE, 10901 N. Torrey Pines Road, La Jolla, CA 92037

Check  Promoter  Beneficial Owner  Executive Officer  Director  General and/or Managing Partner  
Box(es) that Apply:

Full Name (Last name first, if individual)

JOSEPH H. WENDER

Business or Residence Address (Number and Street, City, State, Zip Code)

GSC PARTNERS, 1900 Avenue of the Stars, Ste 2450, Los Angeles, CA 90067

Check  Promoter  Beneficial Owner  Executive Officer  Director  General and/or Managing Partner  
Box(es) that Apply:

Full Name (Last name first, if individual)

C. FRANK BENNETT, PHD

Business or Residence Address (Number and Street, City, State, Zip Code)

ISIS PHARMACEUTICALS, INC., 1896 Rutherford Road, Carlsbad, CA 92008

Check Boxes  Promoter  Beneficial Owner  Executive Officer  Director  General and/or Managing Partner  
that Apply:

Full Name (Last name first, if individual)

DAVID J. ECKER, PHD

Business or Residence Address (Number and Street, City, State, Zip Code)

ISIS PHARMACEUTICALS, INC., 1896 Rutherford Road, Carlsbad, CA 92008

Check Boxes  Promoter  Beneficial Owner  Executive Officer  Director  General and/or Managing Partner  
that Apply:

Full Name (Last name first, if individual)

ARTHUR A. LEVIN, PHD

Business or Residence Address (Number and Street, City, State, Zip Code)

ISIS PHARMACEUTICALS, INC., 1896 Rutherford Road, Carlsbad, CA 92008

Check Boxes  Promoter  Beneficial Owner  Executive Officer  Director  General and/or Managing Partner  
that Apply:

Full Name (Last name first, if individual)

MICHAEL J. TREBLE

Business or Residence Address (Number and Street, City, State, Zip Code)

ISIS PHARMACEUTICALS, INC., 1896 Rutherford Road, Carlsbad, CA 92008

Check Boxes  Promoter  Beneficial Owner  Executive Officer  Director  General and/or Managing Partner  
that Apply:

Full Name (Last name first, if individual)

MARK K. WEDEL, MD, JD

Business or Residence Address (Number and Street, City, State, Zip Code)

ISIS PHARMACEUTICALS, INC., 1896 Rutherford Road, Carlsbad, CA 92008

Check Boxes  Promoter  Beneficial Owner  Executive Officer  Director  General and/or Managing Partner  
that Apply:

Full Name (Last name first, if individual)

Business or Residence Address (Number and Street, City, State, Zip Code)

Check  Promoter  Beneficial Owner  Executive Officer  Director  General and/or Managing Partner  
Box(es) that Apply:

Full Name (Last name first, if individual)

Business or Residence Address (Number and Street, City, State, Zip Code)

**B. INFORMATION ABOUT OFFERING**

1. Has the issuer sold, or does the issuer intend to sell, to non-accredited investors in this offering?..... Yes \_\_\_ No X  
 Answer also in Appendix, Column 2, if filing under ULOE.
2. What is the minimum investment that will be accepted from any individual?..... \$ \_\_\_\_\_ NA
3. Does the offering permit joint ownership of a single unit? ..... Yes \_\_\_ No X
4. Enter the information requested for each person who has been or will be paid or given, directly or indirectly, any commission or similar remuneration for solicitation of purchasers in connection with sales of securities in the offering. If a person to be listed is an associated person or agent of a broker or dealer registered with the SEC and/or with a state or states, list the name of the broker or dealer. If more than five (5) persons to be listed are associated persons of such a broker or dealer, you may set forth the information for that broker or dealer only.

NONE

Full Name (Last name first, if individual)

Business or Residence Address (Number and Street, City, State, Zip Code)

Name of Associated Broker or Dealer

States in Which Person Listed Has Solicited or Intends to Solicit Purchasers NONE  
 (Check "All States" or check individual States).....  All States

[AL]	[AK]	[AZ]	[AR]	[CA]	[CO]	[CT]	[DE]	[DC]	[FL]	[GA]	[HI]	[ID]
[IL]	[IN]	[IA]	[KS]	[KY]	[LA]	[ME]	[MD]	[MA]	[MI]	[MN]	[MS]	[MO]
[MT]	[NE]	[NV]	[NH]	[NJ]	[NM]	[NY]	[NC]	[ND]	[OH]	[OK]	[OR]	[PA]
[RI]	[SC]	[SD]	[TN]	[TX]	[UT]	[VT]	[VA]	[VA]	[WV]	[WI]	[WY]	[PR]

Full Name (Last name first, if individual)

Business or Residence Address (Number and Street, City, State, Zip Code)

Name of Associated Broker or Dealer

States in Which Person Listed Has Solicited or Intends to Solicit Purchasers NONE  
 (Check "All States" or check individual States).....  All States

[AL]	[AK]	[AZ]	[AR]	[CA]	[CO]	[CT]	[DE]	[DC]	[FL]	[GA]	[HI]	[ID]
[IL]	[IN]	[IA]	[KS]	[KY]	[LA]	[ME]	[MD]	[MA]	[MI]	[MN]	[MS]	[MO]
[MT]	[NE]	[NV]	[NH]	[NJ]	[NM]	[NY]	[NC]	[ND]	[OH]	[OK]	[OR]	[PA]
[RI]	[SC]	[SD]	[TN]	[TX]	[UT]	[VT]	[VA]	[VA]	[WV]	[WI]	[WY]	[PR]

Full Name (Last name first, if individual)

Business or Residence Address (Number and Street, City, State, Zip Code)

Name of Associated Broker or Dealer

States in Which Person Listed Has Solicited or Intends to Solicit Purchasers NONE  
 (Check "All States" or check individual States).....  All States

[AL]	[AK]	[AZ]	[AR]	[CA]	[CO]	[CT]	[DE]	[DC]	[FL]	[GA]	[HI]	[ID]
[IL]	[IN]	[IA]	[KS]	[KY]	[LA]	[ME]	[MD]	[MA]	[MI]	[MN]	[MS]	[MO]
[MT]	[NE]	[NV]	[NH]	[NJ]	[NM]	[NY]	[NC]	[ND]	[OH]	[OK]	[OR]	[PA]
[RI]	[SC]	[SD]	[TN]	[TX]	[UT]	[VT]	[VA]	[VA]	[WV]	[WI]	[WY]	[PR]

**C. OFFERING PRICE, NUMBER OF INVESTORS, EXPENSES AND USE OF PROCEEDS**

1. Enter the aggregate offering price of securities included in this offering and the total amount already sold. Enter "0" if answer is "none" or "zero." If the transaction is an exchange offering, check this box  and indicate in the columns below the amounts of the securities offered for exchange and already exchanged.

Type of Security	Aggregate Offering Price	Amount Already Sold
Debt .....	\$ <u>0</u>	\$ <u>0</u>
Equity .....	\$ <u>0</u>	\$ <u>0</u>
<input checked="" type="checkbox"/> Common <input type="checkbox"/> Preferred		
Convertible Securities (including warrants) .....	\$ <u>37,952,500</u>	\$ <u>37,952,500*</u>
Partnership Interests .....	\$ <u>0</u>	\$ <u>0</u>
Other (Specify _____)	\$ <u>0</u>	\$ <u>0</u>
Total .....	\$ <u>37,952,500</u>	\$ <u>37,952,500*</u>

Answer also in Appendix, Column 3, if filing under ULOE.

\*Represents amount receivable by the Issuer upon the exercise of a warrant to purchase common stock (assuming no cashless exercise). Such warrant has not yet been exercised. The Issuer also received a purchase option to later acquire all of Symphony Genlsis Inc.'s equity at a predetermined price.

2. Enter the number of accredited and non-accredited investors who have purchased securities in this offering and the aggregate dollar amounts of their purchases. For offerings under Rule 504, indicate the number of persons who have purchased securities and the aggregate dollar amount of their purchases on the total lines. Enter "0" if answer is "none" or "zero."

	Number Investors	Aggregate Dollar Amount of Purchases
Accredited Investors .....	<u>1</u>	\$ <u>37,952,500</u>
Non-accredited Investors .....	<u>0</u>	\$ <u>0</u>
Total (for filings under Rule 504 only) .....		\$ _____

Answer also in Appendix, Column 4, if filing under ULOE.

3. If this filing is for an offering under Rule 504 or 505, enter the information requested for all securities sold by the issuer, to date, in offerings of the types indicated, in the twelve (12) months prior to the first sale of securities in this offering. Classify securities by type listed in Part C - Question 1.

Type of Offering	Type of Security	Dollar Amount Sold
Rule 505 .....		\$ _____
Regulation A .....		\$ _____
Rule 504 .....		\$ _____
Total .....		\$ _____

4. a. Furnish a statement of all expenses in connection with the issuance and distribution of the securities in this offering. Exclude amounts relating solely to organization expenses of the issuer. The information may be given as subject to future contingencies. If the amount of an expenditure is not known, furnish an estimate and check the box to the left of the estimate.

Transfer Agent's Fees .....	<input type="checkbox"/>	\$ _____
Printing and Engraving Costs .....	<input type="checkbox"/>	\$ _____
Legal Fees .....	<input checked="" type="checkbox"/>	\$ <u>100,000</u>
Accounting Fees .....	<input type="checkbox"/>	\$ _____
Engineering Fees .....	<input type="checkbox"/>	\$ _____
Sales Commissions (specify finders' fees separately) .....	<input type="checkbox"/>	\$ _____
Other Expenses (Identify) _____	<input type="checkbox"/>	\$ _____
Total .....	<input checked="" type="checkbox"/>	\$ <u>100,000</u>

**C. OFFERING PRICE, NUMBER OF INVESTORS, EXPENSES AND USE OF PROCEEDS**

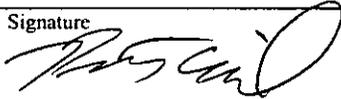
b. Enter the difference between the aggregate offering price given in response to Part C - Question 1 and total expenses furnished in response to Part C - Question 4.a. This difference is the "adjusted gross proceeds to the issuer" ..... \$ 37,852,500

5. Indicate below the amount of the adjusted gross proceeds to the issuer used or proposed to be used for each of the purposes shown. If the amount for any purpose is not known, furnish an estimate and check the box to the left of the estimate. The total of the payments listed must equal the adjusted gross proceeds to the issuer set forth in response to Part C - Question 4.b above.

	Payment to Officers, Directors, & Affiliates	Payment To Others
Salaries and fees.....	<input type="checkbox"/> \$ _____	<input type="checkbox"/> \$ _____
Purchase of real estate.....	<input type="checkbox"/> \$ _____	<input type="checkbox"/> \$ _____
Purchase, rental or leasing and installation of machinery and equipment.....	<input type="checkbox"/> \$ _____	<input type="checkbox"/> \$ _____
Construction or leasing of plant buildings and facilities.....	<input type="checkbox"/> \$ _____	<input type="checkbox"/> \$ _____
Acquisition of other businesses (including the value of securities involved in this offering that may be used in exchange for the assets or securities of another issuer pursuant to a merger).....	<input type="checkbox"/> \$ _____	<input type="checkbox"/> \$ _____
Repayment of indebtedness.....	<input type="checkbox"/> \$ _____	<input type="checkbox"/> \$ _____
Working capital.....	<input checked="" type="checkbox"/> \$ <u>0</u>	<input checked="" type="checkbox"/> \$ <u>37,852,500</u>
Other (specify): _____	<input type="checkbox"/> \$ _____	<input type="checkbox"/> \$ _____
_____	<input type="checkbox"/> \$ _____	<input type="checkbox"/> \$ _____
Column Totals.....	<input checked="" type="checkbox"/> \$ <u>0</u>	<input checked="" type="checkbox"/> \$ <u>37,852,500</u>
Total Payments Listed (column totals added).....	<input checked="" type="checkbox"/> \$ <u>0</u>	<input checked="" type="checkbox"/> \$ <u>37,852,500</u>

**D. FEDERAL SIGNATURE**

The issuer has duly caused this notice to be signed by the undersigned duly authorized person. If this notice is filed under Rule 505, the following signature constitutes an undertaking by the issuer to furnish to the U.S. Securities and Exchange Commission, upon written request of its staff, the information furnished by the issuer to any non-accredited investor pursuant to paragraph (b)(2) of Rule 502.

Issuer (Print or Type) Isis Pharmaceuticals, Inc.	Signature 	Date April 24, 2006
Name of Signer (Print or Type) Patrick R. O'Neil	Title of Signer (Print or Type) Executive Director Legal, Associate General Counsel	

**ATTENTION**

Intentional misstatements or omissions of fact constitute federal criminal violations. (See 18 U.S.C. 1001.)

**END**